REMARKS

Claims 1-20 are pending. Claims 12-14 and 19 have been elected with traverse. Claims 1-11, 15-18 and 20 have been withdrawn.

Claim Rejection – 35 U.S.C. §102

Claims 12 and 19 stand rejected under U.S.C. 102(b) as allegedly anticipated by U.S. Patent No. 5,660,982 to Tryggvason et al. (herein after referred to as "Tryggvason"). In this regard, the Examiner indicates that Tryggvason teaches a method of diagnosing epidermolysis bullosa in a horse including analyzing isolated laminin gamma 2 (γ2)-encoding nucleic acid to identify the presence of mutated nucleic acid having a cytosine insert at position 1368 (as shown in SEQ ID NO:12). Applicant respectfully traverses this rejection of the claims as follows.

Traggvason relates to a variety of methods which include the detection of kalinin/laminin 5 expression in tissue using a probe derived from the gamma-2 (γ2) subunit thereof. These methods are detailed in column 2 of the Tryggvason patent. It should be noted that according to Table 1 (top of column 2) kalinin/laminin 5 is composed of α3β3γ2 chains. It should also be noted that the laminin sequences taught in Tryggvason, and specifically the kalinin/laminin 5 gamma 2 (γ2) nucleic acid sequence from which the probes are derived, are human sequences (see, for example, col. 2, line 26).

At the outset, Applicant points out that the numbering of SEQ ID NO:12 of Tryggvason does not correspond with that in the present application. While nucleotide 1368 is a cytosine in Tryggvason, it forms part of a codon that encodes an amino acid at position 417, while the Tryggvason cytosine that does correspond with the claimed cytosine (1368) occurs at position 1288 in SEQ ID NO:12 of Tryggvason. This alone is sufficient to render the rejection under 35 U.S.C. §102 moot since there is no teaching in Tryggvason of a method of diagnosing EB in horses based on a cytosine insert at nucleic position 1368. Nonetheless, Applicant provides the following further comments.

The Examiner has specifically referred to Example 2 in Tryggvason as allegedly teaching the claimed invention. This example teaches that the occurrence in humans of a homozygous premature termination codon mutation is the specific cause in an examined case of H-JEB (Herlitz phenotype of JEB as set out at col. 3, line 62, not horse JEB). The abnormality in the γ2 laminin subunit was detected by lack of probe binding (col. 7, lines 48-50). Sequencing of the γ2 laminin detected a C to T transition at position 7283 (col. 7, lines 7-16) resulting in a termination codon(TGA) rather than an arginine codon (CGA). Example 1 of Tryggvason also teaches mutations of the γ2 chain gene in cases of human JEB, including a deletion of 219 base pairs from nucleotides 1184-1402 (col. 6, lines 4-5) and a 20 bp deletion and single base pair insertion (col. 6, lines 14-19).

In contrast to the teachings of Tryggvason, the claimed invention relates to a method of diagnosing EB in a horse which comprises identifying the presence of mutated laminin γ2-encoding nucleic acid having a cytosine insert at position 1368.

As set out above, Tryggvason relates to mutations in human laminin γ2 which lead to Herlitz-type JEB. Of the mutations taught in Tryggvason, non relate to the insertion of a cytosine residue at position 1368 of the γ2-encoding nucleic acid sequence. In fact, as shown in Fig. 4A, the normal nucleotide that occurs at position 1368 of human laminin γ2 is cytosine. Thus, Tryggvason could not teach that the identification of this residue is diagnostic of EB in horses as in the claimed invention.

Furthermore, Applicant submits herewith Exhibit #1 an exerpt from the text entitled "Epidermolysis Bullosa" (Fine et al. 1999, The John Hopkins University Press, pages 300-302), which outlines the mutations in the α3, β3 and γ2 polypeptide subunits of laminin-5 (see tables 15-1 and 15-2). This reference establishes that numerous mutations in the LAMA3, LAMB3 and LAMC2 genes were known following the publication of Tryggvason that lead to JEB in humans, none of which corresponds with the mutation described and claimed in the present application, namely a cytosine insert at position 1368 of the LAMC2 gene which affects the amino acid residue at position 391. An IDS

identifying this reference is enclosed. Please deduct the prescribed fee of $180.00 for filing the IDS from the Deposit Account No. 195113.

Applicant acknowledges that the nucleotide homology between the human and horse γ2 chain is undoubtedly high; however, the primers devised using the human sequence do not amplify most of the horse cDNA and genomic LAMC2 DNA sequence. Only the primer pair specific to the horse sequence amplifies the genomic DNA fragment carrying the point mutation at position 1368 which is associated with JEB in the horses as claimed.

Applicants note that several laboratories have tried to use the Tryggvason primers and failed to identify the causative mutation of JEB in horses. Indeed, there is degeneration of two nucleotides in the sense primer and one in the antisense primer between the γ2 sequence in man and horse which prevent correct annealing and amplification of the mutated horse fragment using primers based on the human laminin γ2 sequence of Tryggvason. Accordingly, given the teachings of Tryggvason, i.e. the human laminin γ2 DNA sequence and the primers taught therein, one of skill in the art would not be able to diagnose EB in a horse DNA sample.

In view of the foregoing, Applicant respectfully submits that claim 12 and dependent claim 19 patentably distinguish over the Tryggvason patent and thus, meet the requirements of 35 U.S.C. §102.

Claim Rejections - 35 U.S.C. §103

Claim 12, 14 and 19 stand rejected under 35 U.S.C. §103(a) as allegedly obvious in view of the combined teachings of Tryggvason and U.S. Patent No. 6,265,168 to Gjerde et al. (hereinafter referred to as "Gjerde"). Applicant respectfully traverses this rejection of the claims as follows.

The teachings of Tryggvason have been discussed above.

Gjerde teaches an apparatus and method for separating and purifying

polynucleotides. Gjerde does not teach mutations of laminin γ2-encoding nucleic acid that result in JEB in horses. Accordingly, Applicant submits that Gjerde does not overcome the deficiencies of Tryggvason to teach the claimed invention.

In view of this, Claims 12, 14 and 19 are believed to patentably distinguish over the cited Tryggvason and Gjerde patents and, thus, meet the requirements of 35 U.S.C. §103.

Claim Amendments

Claim 12 has been amended to recite "appropriate sense and antisense primers". This terminology provides a proper antecedent base for these terms in dependent claim 13.

Claim 13 has been amended to define more clearly that the sense primer comprises the recited sequence of SEQ ID NO:29 and that the antisense primer comprises the recited sequence of SEQ ID NO: 30.

SPECIFICATION

The Examiner has noted use of the trademark "QIAQUICK KIT" and requested that it be capitalized and the generic terminology be inserted. Applicant has complied with this request inserting the terminology "DNA purification kit" to generally define the kit.

INFORMATION DISCLOSURE STATEMENT

The Examiner has noted the "References" section of the application indicating that this is not a proper information disclosure statement (IDS) in accordance with MPEP § 609 A(l).

Applicant submitted a proper IDS on June 18, 2002 on a separate sheet as required. A copy of the IDS submitted is enclosed along with a copy of the receipt issued by the USPTO.

CONCLUSION

In view of the foregoing, the application is respectfully submitted to be in condition for allowance, and prompt favourable action thereto is earnestly solicited.

If there are any questions regarding this response or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

Please charge any deficiency in fees or credit any overpayments to Deposit Account No. 195113 (Our File No. P84-US4).

Respectfully submitted,

Date: November 4, 2003

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